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08/468,145 06/06/95 ENGEL Y17506/93-11

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. |
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CUSHMAN DARBY & CUSHMAN
1100 NEW YORK AVENUE NW
NINTH FLOOR EAST TOWER
WASHINGTON DC 20005-3918

MINNIFIELD,N

| EXAMINER | |
|---|---|
| 1645 | |

| ART UNIT | PAPER NUMBER |
|---|---|
| | 07/20/95 |

DATE MAILED:

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

PTO-90C (REV. 2/95)

1-File Copy

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| Office Action Summary | Application No. 08/468,145 | Applicant(s) ENGEL ET AL |
|---|---|---|
| | Examiner N. M. MINNIFELD | Group Art Unit 1645 |

☒ Responsive to communication(s) filed on *Apr 20, 1998* .

☒ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

**Disposition of Claims**

☒ Claim(s) *9, 10, and 12-23* is/are pending in the application.

Of the above, claim(s) *9 and 10* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *12-23* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

**Application Papers**

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. § 119**

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

**Attachment(s)**

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

*--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---*

**DETAILED ACTION**

***Response to Amendment***

1. EFFECTIVE FEBRUARY 7, 1998, the Group and/or Art Unit location of your application in the PTO has changed. In order to expedite the correlation of papers with the application please direct all future correspondence to Technology Center 1600, Group 1640, Art Unit 1645.

2. Applicants' amendment filed April 20, 1998 is acknowledged and has been entered. New claims 20-23 have been added. Claims 12-23 are now pending in the present application. All rejections have been withdrawn, in view of Applicants' amendment, with the exception of those discussed below.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4. Claims 12-19 and now 20-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Callahan et al, Finkenaur (EP 88-308573), Reissman et al and Moore, taken with Sauerbier et al.

Callahan et al teach "...removal of the HF under vacuum, the resin was washed with ether and air dried. The resin was then extracted with 10% HOAc (120 ml), 1% HOAc (120 ml) and water (120 ml). The aqueous extracts were combined, diluted with water and lyophilized to yield 213 mg crude linear peptide. 100 mg crude linear peptide was purified by gel filtration on G-15 with 1% HOAc to yield." (col 13, l. 8-14). The prior art teaches solubilization of heptapeptide in approximately 100-10,000 parts by weight of acetic acid for each part of peptide wherein the

peptide is subsequently transferred to water followed by lyophilization. Finkenaur et al teach a method of lyophilizing a decapeptide in the presence of the bulking agent mannitol. Reissman et al discloses the use of cetrorelix in a pharmaceutical composition. Moore et al teach the conventional method of lyophilization; the lyophilizing peptides of 3-15 amino acids after solubilization in a sufficient amount of acetic acid to form a solution (cols. 7-8). The prior art teaches the claimed invention except for specifically reciting that the product was a sterile lyophilizates.

However, Sauerbier et al teach the lyophilization of a product for use and that this peptide had been sterilized (abstract; claims). Sauerbier et al teach "...sterile filtration of the solution only occurs immediately before filling into injection jars. This ensure greater microbiological safety than does the of sterile crystallizate." (col. 2). Sauerbier et al teaches that the prepared solution is sterilized by filtration using pathogen proof filters conventionally used for this purpose..." (col. 6, l. 41-43).

The claims are directed to a method of preparing a sterile lyophilizates of gel-forming peptide salts by dissolving peptide salts in acetic acid to form a solution, diluting the solution with water, adding a bulking agent, and sterile-filtering the solution, dispensing into vials and lyophilizing the solution.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to incorporate the method of Callahan et al, the addition of the bulking agent mannitol as taught by Finkenaur with the reasonable expectation of success of making a lyophilizate of cetrorelix as taught in Reissmann et al. The prior art teaches the concept of lyophilizing small peptides. It would have been obvious to a person of ordinary skill in the art at the time the invention was made to sterile filter the peptide so that it would be in a sterile for administration to a human; solubilization of peptides after dissolution in acetic acid will result in stabilization of the peptide and therefore greater usefulness in pharmaceutical applications. The claimed invention is prima facie obvious in view of the prior art absent any convincing evidence to the contrary.

Applicant's arguments filed April 20, 1998 have been fully considered but they are not persuasive. Applicants have asserted that Finkenauer would not suggest to one skilled in the art how to make a sterile lyophilisate of the decapeptide Cetrorelix; and that one can not compare a decapeptide with a polypeptide. Applicants have asserted that the prior art does not disclose a medically usable sterile lyophilized Cetrorelix or such a sterile peptide. The method as claimed can be used for any size peptide or polypeptide; it would have been obvious to a person of ordinary skill in the art at the time the invention was made to use the appropriate filter for sterile filtration of a peptide or polypeptide. It would have also been obvious to a person of ordinary skill in the art at the time the invention was made to sterile for the purpose of having a medicinal or pharmaceutical composition to be administered to a patient. Sauerbier et al discloses sterilization via filtration for safety purposes to avoid contamination (col. 2). It is noted that Applicants have argued against the references individually; however, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992).

5. No claims are allowed.

6. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

7. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to N. M. Minnifield whose telephone number is (703) 305-3394. The examiner can normally be reached on Monday-Thursday from 7:00 AM-4:30 PM. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Paula K. Hutzell, Ph.D., can be reached on (703) 308-4310. The fax phone number for this Group is (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

N. M. Minnifield
July 7, 1998

NITA MINNIFIELD
PRIMARY EXAMINER